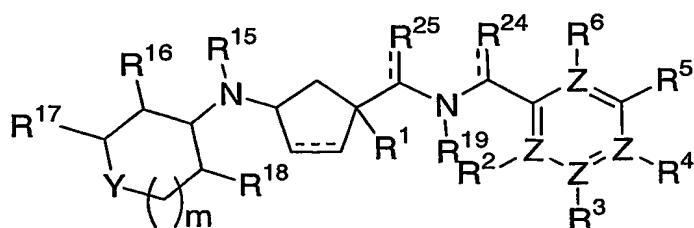
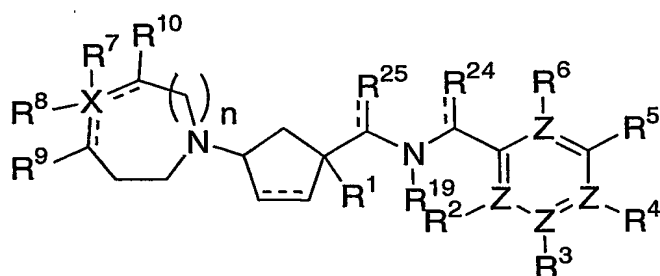


WHAT IS CLAIMED IS:

1. A compound of the formula I or formula II:



I



II

10 wherein:

X is selected from O, N, S, SO₂ and C;

Y is selected from -O-, -NR¹²-, -S-, -SO-, -SO₂-, and -CR¹²R¹²-, -NSO₂R¹⁴-,

15 -NCOR¹³-, -CR¹²COR¹¹-, -CR¹²OCOR¹³-, -CO-;

Z is independently selected from C or N, where at least one Z is N and at most two Z are N;

R¹ is selected from: -C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl, -C₀₋₆alkyl-S-C₁₋₆alkyl, -(C₀₋₆alkyl)-

20 (C₃₋₇cycloalkyl)-(C₀₋₆alkyl), hydroxy, heterocycle, -CN, -NR¹²R¹², -NR¹²COR¹³, -

NR¹²SO₂R¹⁴, -COR¹¹, -CONR¹²R¹², phenyl, and pyridyl,

where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, trifluoromethyl, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -SO₂R¹⁴, -NHCOCH₃, -NHSO₂CH₃, -heterocycle, =O, -CN,

where the phenyl and pyridyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, COR¹¹, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl;

where R¹¹ is independently selected from: hydroxy, hydrogen, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆ alkyl, and trifluoromethyl,

where R¹² is selected from: hydrogen, C₁₋₆ alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and trifluoromethyl,

where R¹³ is selected from: hydrogen, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and trifluoromethyl, and

where R¹⁴ is selected from: hydroxy, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆ cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆ alkyl, and trifluoromethyl;

R² is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₆alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

R³ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

R⁴ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

R⁵ is selected from: C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents selected from fluoro and hydroxyl, -O-C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, -CO-C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, -S-C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, -pyridyl, unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹, fluoro, chloro, bromo, -C₄₋₆cycloalkyl, -O-C₄₋₆cycloalkyl, phenyl, unsubstituted or substituted with one or more substituents selected from:

halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹, -O-phenyl, unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹, -C₃₋₆cycloalkyl, unsubstituted or substituted with 1-6 fluoro, -O-C₃₋₆cycloalkyl, unsubstituted or substituted with 1-6 fluoro, -heterocycle, -CN, and -COR¹¹;

R⁶ is selected from: hydrogen, C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo, phenyl, heterocycle, and nothing, and O, when the Z bonded to R² is N;

- 5 R⁷ is selected from: hydrogen, (C₀₋₆alkyl)-phenyl, (C₀₋₆alkyl)-heterocycle, (C₀₋₆alkyl)-C₃₋₇cycloalkyl, (C₀₋₆alkyl)-COR¹¹, (C₀₋₆alkyl)-(alkene)-COR¹¹, (C₀₋₆alkyl)-SO₃H, (C₀₋₆alkyl)-W-C₀₋₄alkyl, (C₀₋₆alkyl)-CONR¹²-phenyl, (C₀₋₆alkyl)-CONR²⁰-V-COR¹¹, and nothing, when X is O, S, or SO₂,

- 10 where W is selected from: a single bond, -O-, -S-, -SO-, -SO₂-, -CO-, -CO₂-, -CONR¹²- and -NR¹²-,

where V is selected from C₁₋₆alkyl or phenyl,

- 15 where R²⁰ is hydrogen or C₁₋₄alkyl, or where R²⁰ is joined via a 1-5 carbon tether to one of the carbons of V to form a ring,

where the C₀₋₆alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, hydroxy, -C₀₋₆alkyl, -O-C₁₋₃alkyl, trifluoromethyl, and -C₀₋₂alkyl-phenyl,

- 20 where the phenyl, heterocycle, cycloalkyl, and C₀₋₄alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -C₀₋₃-COR¹¹, -CN, -NR¹²R¹², -CONR¹²R¹², and -C₀₋₃-heterocycle,

- 25 or where the phenyl and heterocycle may be fused to another heterocycle, which itself may be unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, -COR¹¹, and -C₁₋₃alkyl, and

where alkene is unsubstituted or substituted with 1-3 substituents which are independently selected from: halo, trifluoromethyl, C₁₋₃alkyl, phenyl, and heterocycle;

5

R⁸ is selected from: hydrogen, nothing when X is either O, S, SO₂ or N or when a double bond joins the carbons to which R⁷ and R¹⁰ are attached, hydroxy, C₁₋₆alkyl, C₁₋₆alkyl-hydroxy, -O-C₁₋₃alkyl, -COR¹¹, -CONR¹²R¹², and -CN;

10 where R⁷ and R⁸ may be joined together to form a ring selected from: 1H-indene, 2,3-dihydro-1H-indene, 2,3-dihydro-benzofuran, 1,3-dihydro-isobenzofuran, 2,3-dihydro-benzothiofuran, 1,3-dihydro-isobenzothiofuran, 6H-cyclopenta[d]isoxazol-3-ol, cyclopentane, and cyclohexane,

15 where the ring formed is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -C₀₋₃-COR¹¹, -CN, -NR¹²R¹², -CONR¹²R¹², and -C₀₋₃-heterocycle, or

where R⁷ and R⁹ or R⁸ and R¹⁰ may be joined together to form a ring which is phenyl or heterocycle,

20

wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -CN, -NR¹²R¹², and -CONR¹²R¹²;

25 R⁹ and R¹⁰ are independently selected from: hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₆alkyl-COR¹¹, C₁₋₆alkyl-hydroxy, -O-C₁₋₃alkyl, =O, when R⁹ or R¹⁰ is connected to the ring via a double bond, and halo;

R¹⁵ is selected from: hydrogen, and C₁₋₆alkyl, unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -CO₂H, -CO₂C₁₋₆alkyl, and -O-C₁₋₃alkyl;

R¹⁶ is selected from: hydrogen, C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents

5 selected from: fluoro, C₁₋₃alkoxy, hydroxyl and -COR¹¹, fluoro, -O-C₁₋₃alkyl, unsubstituted or substituted with 1-3 fluoro, C₃₋₆ cycloalkyl, -O-C₃₋₆cycloalkyl, hydroxy, -COR¹¹, and -OCOR¹³, or R¹⁵ and R¹⁶ are joined together via a C₂₋₄alkyl or a C₀₋₂alkyl-O-C₁₋₃alkyl chain to form a 5-7 membered ring;

10 R¹⁷ is selected from: hydrogen, C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents selected from: fluoro, C₁₋₃alkoxy, hydroxyl and -COR¹¹, COR¹¹, hydroxy, and -O-C₁₋₆alkyl, unsubstituted or substituted with 1-6 substituents selected from: fluoro, C₁₋₃alkoxy, hydroxy, and -COR¹¹, or

15 R¹⁶ and R¹⁷ may be joined together by a C₁₋₄alkyl chain or a C₀₋₃alkyl-O-C₀₋₃alkyl chain to form a 3-6 membered ring;

R¹⁸ is selected from: hydrogen, C₁₋₆alkyl, unsubstituted or substituted with 1-6 fluoro, fluoro, -O-C₃₋₆cycloalkyl, and -O-C₁₋₃alkyl, unsubstituted or substituted with 1-6 fluoro, or

20 R¹⁶ and R¹⁸ are joined together by a C₂₋₃alkyl chain to form a 5-6 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy, or

25 R¹⁶ and R¹⁸ are joined together by a C₁₋₂alkyl-O-C₁₋₂alkyl chain to form a 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy, or

R¹⁶ and R¹⁸ are joined together by a -O-C₁₋₂alkyl-O-chain to form a 6-7 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy;

- 5 R¹⁹ is selected from: hydrogen, phenyl, C₁₋₆alkyl substituted or unsubstituted with 1-6 substituents selected from: -COR¹¹, hydroxy, fluoro, chloro and -O-C₁₋₃alkyl;

- R²⁴ and R²⁵ are independently selected from: =O, where one of R²⁴ and R²⁵ is oxygen bound via a double bond. hydrogen, phenyl, and C₁₋₆alkyl, substituted or unsubstituted with 1-6 substituents selected from: -COR¹¹, hydroxy, fluoro, chloro, -O-C₁₋₃alkyl;
- 10

m is 0, 1 or 2;

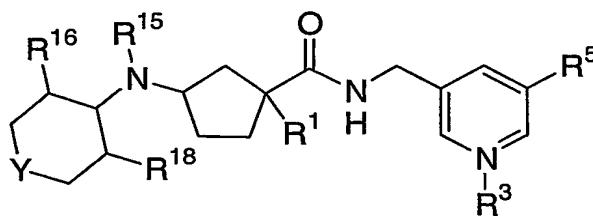
n is 1 or 2;

15

the dashed line represents a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. The compound of claim 1 of the formula Ia:



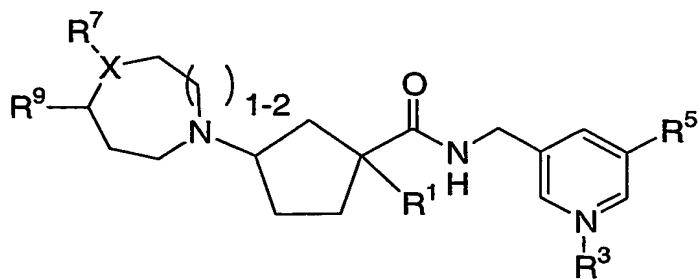
20

Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

25

3. The compound of claim 1 of the formula IIa:

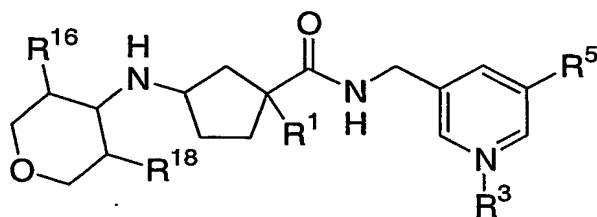


IIa

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

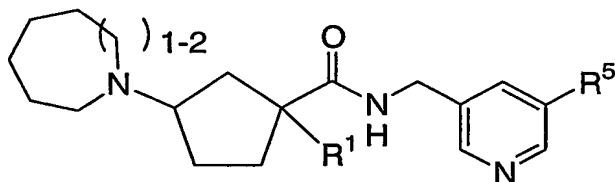
4. The compound of claim 1 of the formula Ib:



Ib

10 and pharmaceutically acceptable salts and individual diastereomers thereof.

5. The compound of claim 1 of the formula IIb:

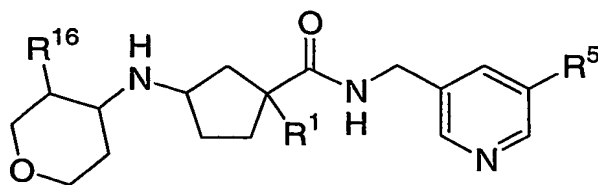


15

IIb

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of claim 1 of the formula Ic:



Ic

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

7. The compound of claim 1, wherein X is C, O or N.

8. The compound of claim 1, wherein X is C.

10

9. The compound of claim 1, wherein Y is $-\text{CH}_2-$ or $-\text{O}-$

15

10. The compound of claim 1, wherein R^1 is selected from: $-\text{C}_{1-6}\text{alkyl}$, $-\text{C}_{0-6}\text{alkyl}-\text{O}-\text{C}_{1-6}\text{alkyl}$, heterocycle, and $-(\text{C}_{0-6}\text{alkyl})-(\text{C}_{3-7}\text{cycloalkyl})-(\text{C}_{0-6}\text{alkyl})$, where the alkyl, heterocycle, and the cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, $-\text{O}-\text{C}_{1-3}\text{alkyl}$, trifluoromethyl, $\text{C}_{1-3}\text{alkyl}$, $-\text{O}-\text{C}_{1-3}\text{alkyl}$, $-\text{COR}^{11}$, $-\text{CN}$, $-\text{NR}^{12}\text{R}^{12}$, and $-\text{CONR}^{12}\text{R}^{12}$.

20

11. The compound of claim 1, wherein R^1 is selected from: $-\text{C}_{1-6}\text{alkyl}$, unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, $-\text{O}-\text{C}_{1-3}\text{alkyl}$, trifluoromethyl, and $-\text{COR}^{11}$; $-\text{C}_{0-6}\text{alkyl}-\text{O}-\text{C}_{1-6}\text{alkyl}$, unsubstituted or substituted with 1-6 substituents independently selected from: halo, trifluoromethyl, and $-\text{COR}^{11}$; and $-(\text{C}_{3-5}\text{cycloalkyl})-(\text{C}_{0-6}\text{alkyl})$, unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, $-\text{O}-\text{C}_{1-3}\text{alkyl}$, trifluoromethyl, and $-\text{COR}^{11}$.

25

12. The compound of claim 1, wherein R^1 is selected from: $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{1-6}\text{alkyl}$ substituted with hydroxyl, and $\text{C}_{1-6}\text{alkyl}$ substituted with 1-6 fluoro.

13. The compound of claim 1, wherein R^1 is selected from: $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{OH})\text{CH}_3$, $-\text{C}(\text{OH})(\text{CH}_3)_2$, and $-\text{CH}_2\text{CF}_3$.

5 14. The compound of claim 1, wherein R^2 is hydrogen.

15. The compound of claim 1, wherein R^3 is nothing.

16. The compound of claim 1, wherein R^4 is hydrogen.

10 17. The compound of claim 1, wherein R^5 is selected from: C_{1-6} alkyl substituted with 1-6 fluoro, $-\text{O}-\text{C}_{1-6}$ alkyl substituted with 1-6 fluoro, chloro, bromo, and phenyl.

15 18. The compound of claim 1, wherein which R^5 is selected from: trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl.

19. The compound of claim 1, wherein R^5 is trifluoromethyl.

20. The compound of claim 1, wherein R^6 is hydrogen.

20 21. The compound of claim 1, wherein R^7 is selected from phenyl, heterocycle, C_{3-7} cycloalkyl, C_{1-6} alkyl, $-\text{COR}^{11}$, and $-\text{CONH}-\text{V}-\text{COR}^{11}$, where V is selected from C_{1-6} alkyl and phenyl, and where the phenyl, heterocycle, C_{3-7} cycloalkyl, and C_{1-6} alkyl is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C_{1-3} alkyl, $-\text{O}-\text{C}_{1-3}$ alkyl, $-\text{COR}^{11}$, $-\text{CN}$, heterocycle, and $-\text{CONR}^{12}\text{R}^{12}$.

22. The compound of claim 1, wherein, when X is not O, R^7 is selected from phenyl, heterocycle, C_{1-4} alkyl, $-\text{COR}^{11}$ and $-\text{CONH}-\text{V}-\text{COR}^{11}$, where V is selected from C_1 -

alkyl or phenyl, where the phenyl, heterocycle, and C₁₋₄alkyl is unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, and -heterocycle.

- 5 23. The compound of claim 1, wherein X is O, and R⁷ and R⁸ are nothing.
24. The compound of claim 1, wherein X is C, and R⁸ is hydrogen.
25. The compound of claim 1, wherein which R⁹ is selected from: hydrogen,
10 hydroxy, -CH₃, -O-CH₃, and =O, where R⁹ is joined to the ring via a double bond.
26. The compound of claim 1, wherein R⁹ is hydrogen.
27. The compound of claim 1, wherein R¹⁰ is hydrogen.
- 15 28. The compound of claim 1, wherein R¹⁵ is hydrogen or methyl.
29. The compound of claim 1, wherein R¹⁶ is selected from: hydrogen,
C₁₋₃alkyl, unsubstituted or substituted with 1-6 fluoro, -O-C₁₋₃alkyl, fluoro, and hydroxy.
- 20 30. The compound of claim 1, wherein R¹⁶ is selected from: hydrogen,
trifluoromethyl, methyl, methoxy, ethoxy, ethyl, fluoro, and hydroxy.
31. The compound of claim 1, wherein R¹⁷ is hydrogen.
- 25 32. The compound of claim 1, wherein R¹⁸ is selected from: hydrogen,
methyl, and methoxy.
33. The compound of claim 1, wherein R¹⁸ is hydrogen.

34. The compound of claim 1, wherein R¹⁶ and R¹⁸ are joined together by a -CH₂CH₂- chain or a -CH₂CH₂CH₂- chain to form a cyclopentyl ring or a cyclohexyl ring.

5 35. The compound of claim 1, wherein R¹⁹ is hydrogen.

36. The compound of claim 1, wherein R²⁴ is hydrogen.

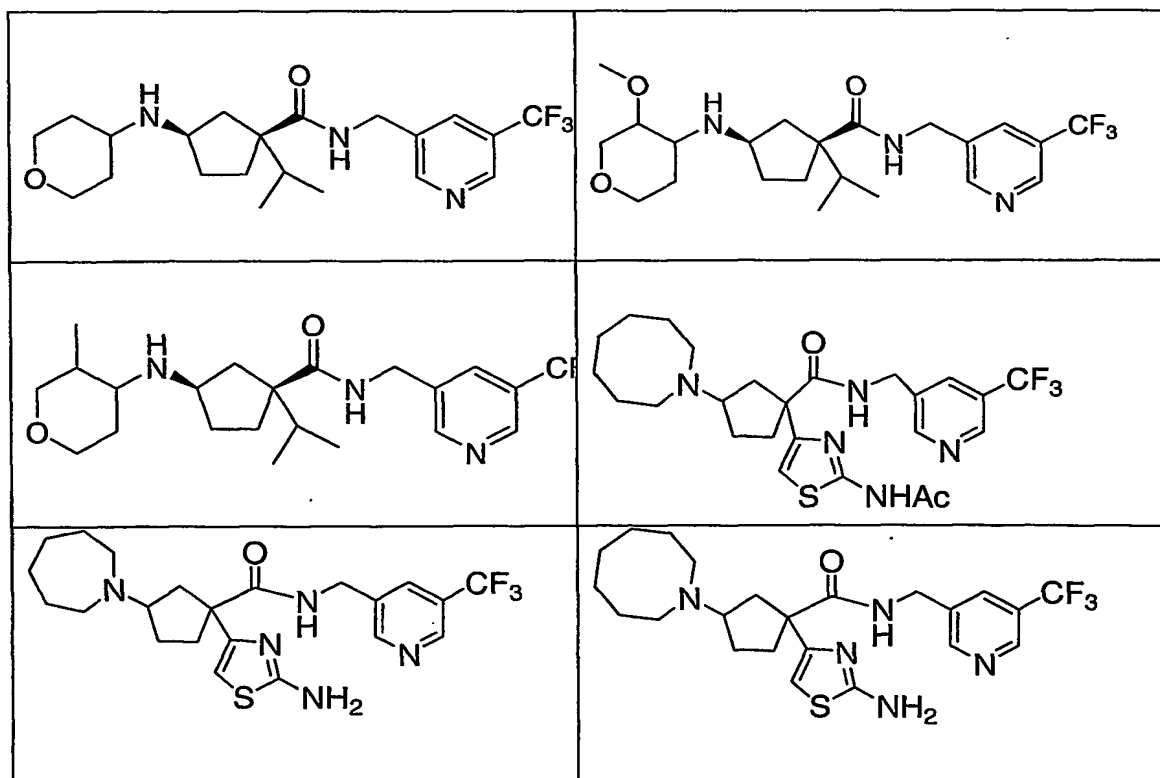
37. The compound of claim 1, wherein R²⁵ is =O.

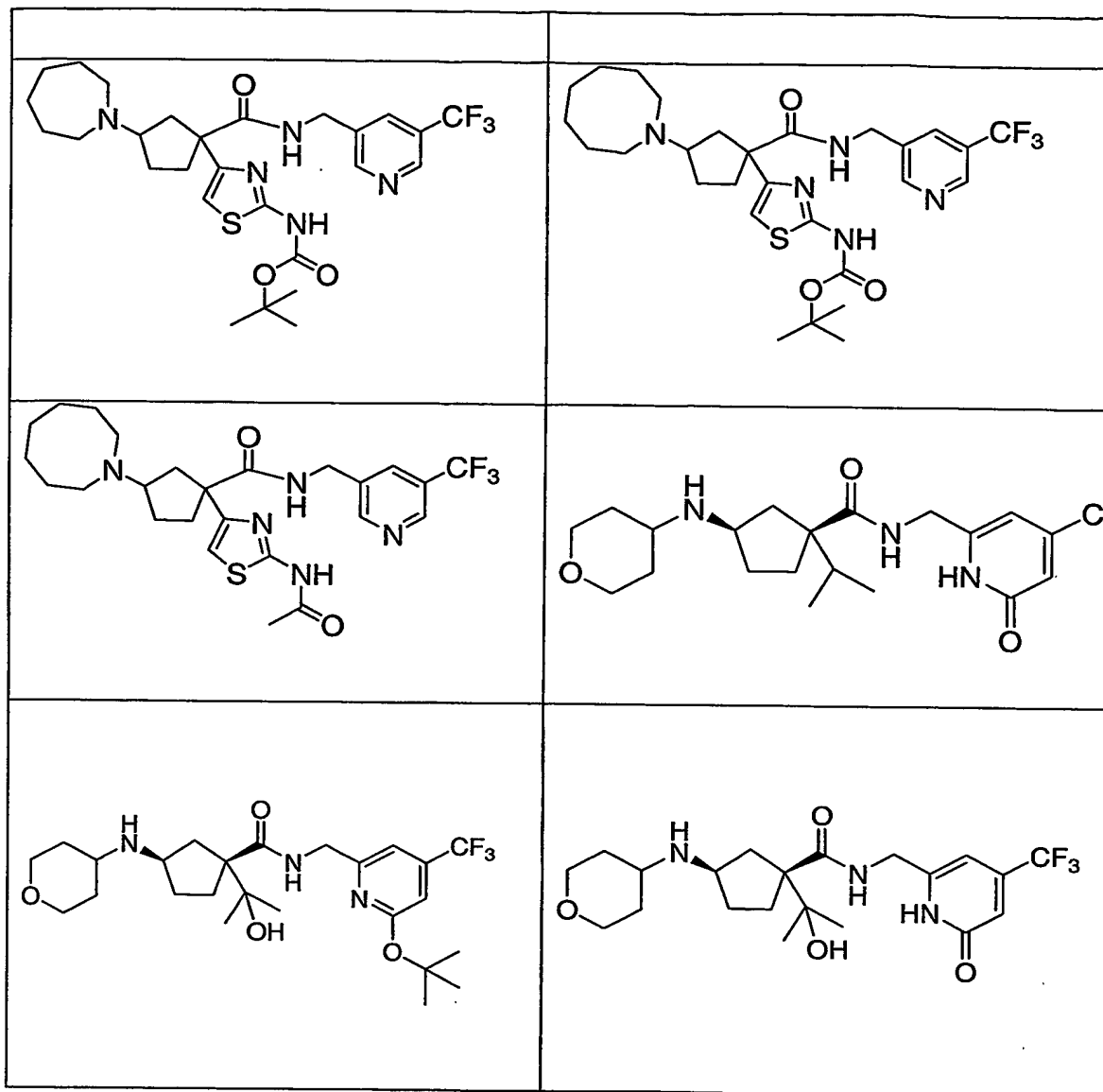
10

38. The compound of claim 1, wherein m = 0 or 1.

39. The compound of claim 1, wherein n = 1 or 2.

15 40. A compound selected from:





41. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

5 42. A method for modulation of chemokine receptor activity in a mammal which comprises the administration of an effective amount of a compound of Claim 1.

43. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the administration to a patient of an effective amount of a compound of Claim 1.

5

44. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of a compound of Claim 1.